frequency mode corresponds to the CCC bend (476 cm^{-1}). The out-of-plane bending modes of the CH_2 group in the allyl radical have lower frequencies (786 and 761 cm^{-1}) than the same mode in propene (959 cm^{-1}) but higher frequency than the pyramidal motion of the radical center in the ethyl radical. These out-of-plane bending motions are predicted to be responsible for a very intense band near 770 cm^{-1} characteristic of the IR spectrum of the allyl radical. Previously, we had reported that the lowest frequency mode in the cyclopropyl radical was the α CH bending model (713 cm^{-1}). The allyl radical has several vibrational modes with lower or similar frequency. The present study should be valuable for the identification of the spectra of the allyl radical and of the cyclopropyl radical.

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Registry No. CH_2CHCH_2 radical, 1981-80-2; CH_2CDCH_2 radical, 78370-41-9; CD_2CHCD_2 radical, 84752-87-4; CD_2CDCD_2 radical, 84752-88-5; $CH_3CH{=}CH_2$, 115-07-1; $CH_3CD{=}CH_2$, 1184-59-4; $CH_3CH{=}CD_2$, 1517-49-3; $CD_3CH{=}CH_2$, 1517-51-7.

Treatment of Electrostatic Effects within the Molecular Mechanics Method.[1] 1

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Abstract: A model of intramolecular electrostatic effects (called the induced dipole moment and energy (IDME) method) was derived by extending the method originally proposed by Del Re for calculating dipole moments and charge distributions. The IDME procedure consists of taking bond dipoles, calculated by the Del Re procedure, and allowing for nonadjacent dipole interactions by taking all components of bond polarizabilities into account. The method is applied to some simple halides, ketones, and ethers. The total dipole moments are well calculated and charge distributions reproduce many known trends. The calculated energies agree better with experiment overall than those calculated earlier by the modified Smith–Eyring method.

Molecular mechanics calculations have been developed to a high degree of sophistication for hydrocarbons.[2] Similar reasonably accurate and detailed studies have also been carried out for monofunctional polar compounds.[3-8] While the results here are less accurate than for hydrocarbons, they are sufficiently good as to show promise for the general method.

With molecules containing two or more neighboring polar groups, believable molecular mechanics calculations necessitate that electrostatic interactions be considered in addition to what is done with more simple molecules. The differences between predicted and observed equilibrium constants have often been used to estimate the magnitude of such interactions[9] and suggest important effects in 4-hydroxy-[10] and 4-chlorocyclohexanone,[11] for instance. The importance of electrostatic interactions is also evidenced by the strong phase and solvent dependence of conformational equilibria for a number of compounds. Hydrocarbons are known as nonpolar and quite insensitive to phase and solvent as far as their structural properties and conformational energies are concerned.[12] On the other hand, for molecules containing neighboring polar groups, conformational energies may be very sensitive to phase and solvent. 1,2-Dichloroethane, for example, is a mixture of gauche and anti conformations.[13] The composition of the mixture is strongly dependent upon phase and solvent. In the 5-heterosubstituted 1,3-dioxanes,[14] the ΔG for the axial vs. equatorial position of the 5-substituent varies by about 1 kcal/mol on going from the slightly polar carbon tetrachloride to the highly polar acetonitrile. Therefore, in order to apply molecular mechanics to polyfunctional polar compounds in a useful way, electrostatic and solvation interactions must somehow be taken into account.

Previously the electrostatics of the system has been treated in terms of either point dipoles or point charges, utilizing a medium of effective dielectric constant in a standard way.[2] Such models are approximations that we expect to be accurate if the distance between charges (dipoles) in different bonds is large, or at least large compared to the diameters of the atoms or to the effective distance between charges in the same bond. With a few significant exceptions, the two methods (charges or dipoles) give results that are substantially the same. Neither was able to explain, for instance, the high experimental value of the dipole moment of 2β,3α-dichloro-5-cholestane[15] and of a number of other 1,2-diaxial dihalides.

A method for treating the problem of induction, dealing with charges on the classical level, was long ago developed by Smith

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(1) The work was supported in part by the Republic Research Fund, SR Serbia. Abstracted from the Ph.D. thesis of L.D.-M. submitted to the University of Belgrade, 1979.

(2) J. E. Williams, P. J. Stang, and P. von R. Schleyer, *Annu. Rev. Phys. Chem.*, **19**, 531 (1968); C. Altona and D. H. Faber, *Top. Curr. Chem.*, **45**, 1 (1974); N. L. Allinger, *Adv. Phys. Org. Chem.*, **13**, 1 (1976); O. Ermer, *Struct. Bonding (Berlin)*, **27**, 161 (1976); D. N. J. White and M. Bovill, *J. Chem. Soc., Perkin Trans. 2*, 1610 (1977); A. Warshel, *Mod. Theor. Chem.*, **7**, 133 (1978); L. S. Bartell, *J. Am. Chem. Soc.*, **99**, 3279 (1977); S. Fitzwater and L. S. Bartell, *ibid.*, **98**, 5107 (1976); N. L. Allinger, *ibid.*, **99**, 8127 (1977).
(3) N. L. Allinger and D. Y. Chung, *J. Am. Chem. Soc.*, **98**, 6798 (1976).
(4) N. L. Allinger and M. J. Hickey, *J. Am. Chem. Soc.*, **97**, 5167 (1975).
(5) N. L. Allinger and J. Kao, *Tetrahedron*, **32**, 529 (1976).
(6) N. L. Allinger, M. J. Hickey, and J. Kao, *J. Am. Chem. Soc.*, **98**, 2741 (1976); N. L. Allinger, J. Kao, H. Chang, and D. B. Boyd, *Tetrahedron*, 32, 2867 (1976).
(7) A. Y. Meyer and N. L. Allinger, *Tetrahedron*, **31**, 1971 (1975).
(8) N. L. Allinger and H. Chang, *Tetrahedron*, **33**, 1561 (1977).
(9) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Wiley-Interscience, New York, 1965.
(10) R. D. Stolow and T. Groom, *Tetrahedron Lett.*, **4069** (1968).
(11) D. N. Kirk, *Tetrahedron, Lett.*, 1727 (1969).
(12) R. A. Ford and N. L. Allinger, *J. Org. Chem.*, **35**, 3178 (1970); R. J. Ouellette and S. Williams, *J. Am. Chem. Soc.*, **93**, 466 (1971).
(13) S. I. Mizushima, "Structure of Molecules and Internal Rotation", Acedemic Press, New York, 1954.
(14) R. J. Abraham, H. D. Banks, E. L. Eliel, O. Hofer, and M. K. Kaloustian, *J. Am. Chem. Soc.*, **94**, 1913 (1972).
(15) H. J. Geise, A. Tieleman, and E. Havinga, *Tetrahedron*, **22**, 183 (1966).

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Table 1. Dipole Moments

compound	calculated IDME	calculated MSE	observed[a]
CH_3F	1.95	1.59	1.82[f]
CH_2F_2	2.03	1.63	1.96
CHF_3	1.56	1.25	1.62[f]
CF_4	0.00	0.00	0.0
CH_3CH_2F	2.0	1.67	1.95[f]
CH_3CF_3	2.36	1.85	2.31[f]
CH_3Cl	1.97	1.95	1.94
CH_2Cl_2	1.75	1.65	1.54-2.39
$CHCl_3$	0.99	1.06	1.03
CH_3CH_2Cl	2.13	2.10	2.04
CH_3CHCl_2	2.32	1.99	2.07, 2.69
CH_3CCl_3	1.96	1.68	1.79, 2.03
1,1-dichloro-cyclohexane	3.06	2.36	2.48[d]
$(CH_3)_3CCl$	2.23		2.06, 2.13
CH_3Br	1.84	1.81	1.79
$CHBr_3$	0.92	0.93	1.00
CH_3CH_2Br	2.04	1.95	1.94
HOH	1.96	0.06	1.82
CH_3OH	1.63	1.69	1.70
CH_3OCH_3	1.38	1.39	1.31,[f] 1.25[b]
tetrahydrofuran	1.63	1.72	1.63
tetrahydropyran	1.51	1.56	1.63,[e] 1.69[f,b]
1,3-dioxane	2.21	2.11	2.14,[c] 2.13[b]
1,3-dioxolane (half-chair)	1.13		
1,3-dioxolane (envelope)	1.66		1.47[b]
HCHO	2.48	2.26	2.28[f]
CH_3CHO	2.71	2.67	2.70,[f] 2.51[b]
$(CH_3)_2CO$	2.83	2.89	2.86[f]
cyclohexanone	3.04	2.99	3.08[f]

[a] Dipole moments are for the gas phase unless otherwise stated.[37] [b] Dipole moment of the compound itself measured in the benzene solution. [c] In the cyclohexane solution. [d] In the carbon tetrachloride solution. [e] Dipole moment of a pure liquid. [f] Average value.

and Eyring[16] and applied to numbers of problems. Although the Smith–Eyring (SE) method accounted adequately for charge interactions between atoms bound to a common atom, in its original form it took no account of interactions between nonadjacent bonds. A modified version of the Smith–Eyring method (MSE) that does take these interactions into account was developed more recently.[17]

A number of authors who have studied the influence of substituents on reaction rates have emphasized the importance of induction,[18] but the models developed to calculate this effect require empirical parameters to be determined for each particular substituent.[19] In any case, the general conclusion is that the field effect, i.e., interactions between nonadjacent dipoles (charges), has to be accounted for when treating induction in a molecule.

In earlier papers[17,22] we modified the SE (Smith–Eyring)[16] method by including terms to account for these nonadjacent interactions (MSE method). The method was quite successful for the calculation of molecular dipole moments (Table I) but only moderately so for conformational energies. It was impossible, for example, to calculate simultaneously and correctly the dipole moments and conformational energies of the 2-halocyclohexanones and the 2,6-dihalocyclohexanones[22] (Table II). The MSE method allows for induction along bonds (longitudinal polarizability), but not perpendicular to them (transverse and vertical polarizabilities). It was thought that the neglect of these latter polarizabilities might have been a major reason for this discrepancy. On the other hand, it was not possible to introduce transverse and vertical polarizabilities into the treatment of induction in the MSE method. The MSE method is based on atomic charges, which are not influenced by the transverse and vertical components of an induced bond dipole. Bond dipoles, to which it would be possible to assign all three components of the bond polarizability, could not be uniquely derived from the net atomic charges. Therefore in the present work we have utilized an alternative approach to the problem, introduced originally by Del Re,[20] where bond dipole moments arising from inductive effects of adjacent bonds were readily obtained. The IDME (induced dipole moment and energy) method was developed to account for interactions between nonadjacent polar groups by considering all of the components of the induced dipoles and their mutual interactions. This procedure provides a more complete treatment of the electrostatics of molecules. Combining the molecular mechanics[21] method and the earlier described treatment of solvation,[22] we would hope to be able to make reliable predictions of dipole moments and conformational energies of polyfunctional polar compounds, both in the gas phase and in reasonably indifferent solvents with dielectric constants ranging from 2 to about 30.

IDME (Induced Dipole Moment and Energy) Method

The dipole of a polarizable bond, which is considered as a point dipole located at the "bond center corresponding to the covalent radii", i.e., at the point of a maximum electron density (point C, see diagram), may be represented by

$$\mu_i = \mu^\circ_i + \mu^i_i \tag{1}$$

where μ_i is the resultant dipole moment of bond i, μ°_i is the permanent dipole moment of bond i, and μ^i_i is the induced dipole moment of bond i.

The distance JC is

$$R_{JC} = (R_J/(R_J + R_P))R_{JP}$$

where R_J,R_P are the covalent radii of atoms J and P, and R_{JP} is the J–P bond length.

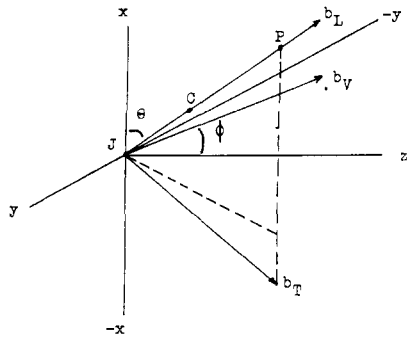
The induced dipole moment is given by eq 2, where $\mathbf{E}_j$ =

$$\mu^i_i = -\alpha_i \mathbf{E}_j = -\alpha_i \sum_{\substack{j=1 \\ j\neq i}}^{n} \mathbf{T}_{ij}\mu_j \tag{2}$$

$\sum_{j=1,j\neq i}^{n} \mathbf{T}_{ij}\mu_j$ is an electrostatic field of all of the dipoles in the molecule except dipole i, n is the number of bonds (dipoles) in the molecule, α_i is a bond polarizability tensor, and $\mathbf{T}_{ij}$ is the dipole field tensor.

The bond polarizabilities available in the literature[23] are longitudinal, transverse, and vertical, placed along the principal axes of the bond. In order to consider interactions between two polarizable bonds, their polarizabilities have to be expressed in the same coordinate system. The coordinate system we chose, in common to all the bonds in the molecule, was a Cartesian coordinate system fixed with respect to the molecule. The relationship between the coordinate system of one bond and the common coordinate system is given in the following diagram. The b_L is the axis of the longitudinal bond polarizability that passes through the bond JP and makes an angle θ with the positive direction of the x axis. The b_T, transverse bond polarizability, is defined to be in the plane of x and b_L axes and to form an acute angle with the negative direction of the x axis. The b_V, vertical bond polarizability, which is perpendicular to both b_L and b_T, has such a direction that a right-handed Cartesian coordinate system

(16) R. P. Smith, T. Ree, J. L. Magee, and H. Eyring, *J. Am. Chem. Soc.*, **72**, 2263 (1951); R. P. Smith and H. Eyring, *ibid.*, **74**, 229 (1952); R. P. Smith and E. M. Mortensen, *ibid.*, **78**, 3932 (1956); R. P. Smith and J. J. Rasmussen, *ibid.*, **83**, 3785 (1961).
(17) N. L. Allinger and M. Wuesthoff, *Tetrahedron*, **33**, 3 (1977).
(18) F. W. Baker, R. C. Parish, andd L. M. Stock, *J. Am. Chem. Soc.*, **89**, 5677 (1967); M. J. S. Dewar and P. J. Grisdale, *ibid.*, **84**, 3539 (1962), C. L. Liotta, W. F. Fisher, G. H., Greene, Jr., and B. L. Joyner, *ibid.*, **94**, 4891 (1972); L. M. Stock, *J. Chem. Educ.*, **49**, 400 (1972); T. W. Cole, Jr., C. J. Mayers, and L. M. Stock, *J. Am. Chem. Soc.*, **96**, 4555 (1974); R. W. Taft and C. A. Grob, *ibid.*, **96**, 1236 (1974).
(19) M. J. S. Dewar, R. Golden, and J. M. Harris, *J. Am. Chem. Soc.*, **93**, 4187 (1971).
(20) G. Del Re, *J. Chem. Soc.*, 4031 (1958).
(21) N. L. Allinger, *J. Am. Chem. Soc.*, **99**, 8127 (1977).
(22) L. Došen-Mičović and N. L. Allinger, *Tetrahedron*, **34**, 3385 (1978).
(23) R. J. LeFèvre, *Adv. Phys. Org. Chem.*, **3**, 1 (1965).



is formed. It is obvious that the b_V axis is in the zy plane. The angle formed by rotating the positive z axis until it is parallel to b_V and in such a direction that a right-handed screw progresses along the positive x axis is denoted by Φ.

The polarizability tensor α, which in a bond coordinate system has a form:

$$a = \begin{bmatrix} b_L & 0 & 0 \\ 0 & b_T & 0 \\ 0 & 0 & b_V \end{bmatrix}$$

in a Cartesian coordinate system fixed with respect to the molecule becomes $\mathbf{D}\alpha\mathbf{D}^{-1}$, where $\mathbf{D}$ represents the transformation of the direction cosine matrix[24] relating the bond coordinate system to the Cartesian coordinate system fixed with respect to the molecule.

The equations derived are similar to the ones given by Silberstein[25] and developed and used later by Mortensen[26] and Applequist, Carl, and Fung[27] for the calculations of the molecular polarizability tensor. The difference is that instead of having an applied external field as in their calculations, we have an internal field produced by permanent and induced bond dipoles.

When developed for the n bonds in the molecule, eq 2 may be represented by a matrix equation where $\mathbf{I}$ is the unit matrix:

$$\begin{bmatrix} 1 & \alpha_1 T_{1,2} & \cdots & \alpha_1 T_{1,n} \\ \alpha_2 T_{2,1} & 1 & & \alpha_2 T_{2,n} \\ \vdots & & & \\ \alpha_n T_{n,1} & & \cdots & 1 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \\ \vdots \\ \mu_n \end{bmatrix} = \begin{bmatrix} \mu^0_1 \\ \mu^0_2 \\ \vdots \\ \mu^0_n \end{bmatrix} \quad (3)$$

or briefly:

$$\mathbf{A}\mu = \mu^0 \quad (4)$$

where $\mathbf{A}$ is the $3n \times 3n$ matrix in eq 3 and μ and μ^0 are corresponding $3n \times 1$ column vectors.

Let $\mathbf{B} = \mathbf{A}^{-1}$; here $\mathbf{B}$ is a $3n \times 3n$ matrix with elements B_{ij}. From eq 4 it follows that

$$\mu = \mathbf{B}\mu^0$$

or

$$\begin{bmatrix} \mu_{1x} \\ \mu_{1y} \\ \mu_{1z} \\ \cdot \\ \cdot \\ \cdot \\ \mu_{nx} \\ \mu_{ny} \\ \mu_{nz} \end{bmatrix} = \begin{bmatrix} B_{1,1} & B_{1,2} & \cdots & B_{1,3n} \\ B_{2,1} & B_{2,2} & \cdots & B_{2,3n} \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ B_{3n,1} & & \cdots & B_{3n,3n} \end{bmatrix} \begin{bmatrix} \mu^0_{1x} \\ \mu^0_{1y} \\ \mu^0_{1z} \\ \cdot \\ \cdot \\ \cdot \\ \mu^0_{nx} \\ \mu^0_{ny} \\ \mu^0_{nz} \end{bmatrix} \quad (5)$$

which is equivalent to the $3n$ equations of the type

$$\mu_{ix} = \sum_{j=1, j\neq i}^{n} (B_{3i-2,3j-2}\mu^0_{jx} + B_{3i-2,3j-1}\mu^0_{jy} + B_{3i-2,3j}\mu^0_{jz})$$

$$\mu_{iy} = \sum_{j=1, j\neq i}^{n} (B_{3i-1,3j-2}\mu^0_{jx} + B_{3i-1,3j-1}\mu^0_{jy} + B_{3i-1,3j}\mu^0_{jz}) \quad (6)$$

$$\mu_{iz} = \sum_{j=1, j\neq i}^{n} (B_{3i,3j-2}\mu^0_{jx} + B_{3i,3j-1}\mu^0_{jy} + B_{3i,3j}\mu^0_{jz})$$

From this system of equations it is possible to deduce bond dipole moments:

$$\mu_i = (\mu_{ix}^2 + \mu_{iy}^2 + \mu_{iz}^2)^{1/2} \quad (7)$$

as well as the molecular dipole moment, which for a molecule of n bonds is

$$\mu = [(\sum_{i=1}^{n}\mu_{ix})^2 + (\sum_{i=1}^{n}\mu_{iy})^2 + (\sum_{i=1}^{n}\mu_{iz})^2]^{1/2} \quad (8)$$

If q_i is a total net charge on atom i, and Q^j_i is the net charge on atom i due to the polarization of the bond i–j, then

$$q_i = \sum_j Q^j_i \quad (9)$$

Equation 9 enables calculation of the charge distribution in the molecule. The Q^j_i is:

$$Q^j_i = \mu^1_{ij}/R_{ij} \quad (10)$$

R_{ij} being bond length and μ^1_{ij} being the longitudinal component of the i–j bond dipole moment. The μ^1_{ij} is readily obtained from the x, y, z components of dipole moment and the known molecular geometry.

The energy of interaction of two dipoles μ_1 and μ_2 may be represented by

$$W_{1,2} = \mu_1 T_{1,2} \mu_2 \quad (11)$$

The energy of interaction of two charges is given by

$$W_{ij} = q_i q_j / \epsilon R_{ij} \quad (12)$$

where R_{ij} is the distance between charges. Summation over all the interactions in the molecule gives the total dipolar (charge) interaction energy.

In the IDME method, mutual induction and interactions between nongeminal bonds (the through-space induction) have been considered. Consideration of interactions between geminal bonds (the through-bond induction) was included in the calculation of μ^0, "the permanent bond dipole".

The procedure is as follows: the previously described Del Re method[20] (utilizing somewhat changed parameters) was used to consider induction through bonds and to calculate bond dipole moments arising from inductive effects of the bonds joined to a common atom. These bond dipole moments are taken to be "permanent dipole moments". In the IDME method they are allowed to interact with dipoles of nonadjacent bonds and the resulting dipole moments and interaction energies are calculated.

The Del Re method was convenient to use since it has a quantum mechanical basis and, on the other hand, it uses bond charges and dipoles, which are suitable for use with molecular mechanics methods. At the same time its parameter set was teested with respect to the molecular dipole moments.

Origin and Determination of the Parameters

The application of the simple MO–LCAO method to the calculation of bond charges implies, in principle, the solution of the secular equation. For a localized bond between atoms P and J this equation is

$$\begin{vmatrix} H_{PP} - E & H_{PJ} - ES_{PJ} \\ H_{PJ} - ES_{PJ} & H_{JJ} - E \end{vmatrix} = 0 \quad (13)$$

where H_{PP} is the Coulomb integral, H_{PJ} is the resonance integral, S_{PJ} is the overlap integral, and E is the energy. Overlap (S_{PJ}) is often neglected. The nature of the simple MO–LCAO method requires that the other three parameters, H_{PP}, H_{JJ}, and H_{PJ}, should

(24) R. P. Smith and E. M. Mortensen, *J. Chem. Phys.* **32**, 502 (1959).
(25) L. Silberstein, *Philos. Mag.*, 33, 92, 215, 521 (1917).
(26) E. M. Mortensen, *J. Chem. Phys.*, **49**, 3732 (1968).
(27) J. Applequist, J. R. Carl, and K. K. Fung, *J. Am. Chem. Soc.*, **94**, 2952 (1972).

Table II. Dipole Moments and Conformational Energies

compounds		dipole moments MSE	IDME	exptl	conformational energies[a] ΔE, kcal/mol MSE	IDME	exptl[f] 1R	UV	dm	kc	NMR	NMR
2-fluorocyclohexanone	a	2.83	2.84	2.95[b]								
	e	4.15	4.24	4.35	0.26	0.39			0.05		0.17	
2-chlorocyclohexanone	a	3.04	3.05	3.17[b]								
	e	4.35	4.16	4.29	−0.50	−0.40	−0.50	−0.31	−0.68	−0.31[e]	−0.74	−0.19
2-bromocyclohexanone	a	3.02	3.12	3.20[b]								
	e	4.14	4.07	4.27	−0.79	−0.74			−1.03	−0.78[e]	−1.28	−0.68
cis-2,6-difluorocyclohexanone	aa	3.42	3.57									
	ee	4.82	4.79		0.22	1.89	large + *g*					
cis-2,6-dichlorocyclohexanone	aa	4.06	3.88									
	ee	5.01	4.76	4.84[c]	0.62	1.67	1.74[g]					
cis-2,6-dibromocyclohexanone	aa	3.98	3.93									
	ee	4.73	4.68	4.76[c]	0.23	1.02	1.03[g]					
cis-1,3-dibromocyclohexane	aa	3.66	3.51									
	ee	2.24	2.35	2.19[h,j]	3.04	4.49					>2.0[h]	
r-1-*c*-3-dichloro-*t*-5-methylcyclohexane	aa	3.95	3.77									
	ee	2.38	2.56	2.48[i,j]	0.57	1.67					1.30[i]	

[a] $\Delta E = E_a - E_e$ or $E_{aa} - E_{ee}$. [b] Dipole moments of the corresponding halo-4-*tert*-butyl compounds.[39] [c] Dipole moments of the corresponding dihalo-4-*tert*-butyl compounds.[40] [d] Solvent C_6H_{12}.[41] [e] Solvent C_6H_{12}, ref 42 and references cited therein. [f] Reference 22 solvent C_6H_{12}, and references cited therein unless otherwise stated. [g] Solvent CCl_4.[43] [h] Reference 48. [i] Reference 49. [j] Dipole moment of the compound itself.

be evaluated empirically on the basis of the nature of the atoms involved in the bond and of their surroundings. The Del Re method starts from the equations

$$H_{PP} = \eta + \delta_P\beta$$
$$H_{JJ} = \eta + \delta_J\beta \qquad (14)$$
$$H_{PJ} = \nu_{PJ}\beta$$

where η and β are basic parameters whose values need not be known. The assumption was made that to a first approximation ν_{PJ} was independent of surroundings, while δ_P and δ_J were influenced only by atoms directly bound to P and J, respectively. According to these assumptions an expression for δ_P should be

$$\delta_P = \delta^\circ_P + \sum_{\substack{K\ adj \\ to\ P}} \gamma_{P(K)}\delta_K \qquad (15)$$

where δ°_P and $\gamma_{P(K)}$ are two suitable parameters, one depending only upon the nature of atom P, the other upon atom P and each adjacent atom K.

When δ's for N atoms in the molecule are evaluated, bond charges (Q) and consequently bond dipoles may be derived from 20

$$Q_{PJ} = (\delta_J - \delta_P)/2\nu_{PJ} \qquad (16)$$

Thus there are five parameters used to describe one bond (J–P): ν_{JP}, $\gamma_{J(P)}$, $\gamma_{P(J)}$, δ°_J, and δ°_P. The quantities δ°_J and δ°_P are correlated with electronegativities (EN) by

$$\delta^\circ_J = c(EN_J - EN_H)/EN_H \qquad (17)$$

where c is a proportionality constant that was determined by fitting calculated to experimental dipole moments. The next step was to choose values for γ. The only clues for these were the parameters used for π systems. It was suggested[20] that the quantity corresponding to γ had a value equal to 0.1 for the effect of heteroatoms on carbon. Therefore, it has been assumed[20] that the values of γ should be that order of magnitude. The cases of CH_3Cl and $(CH_3)_3CCl$ were also considered. The condition that $(\delta_{Cl} - \delta_C)$ in the later should be larger than that in the former was imposed because of the known order of the inductive effects of the methyl and *tert*-butyl groups. This led to the conclusion that the two conditions to be fulfilled were

$$\gamma_{H(C)}\gamma_{C(C)} > \gamma_{C(C)}$$
$$\gamma_{C(Cl)}/\gamma_{Cl(C)} \gg \delta^\circ_C/\delta^\circ_{Cl} \qquad (18)$$

Values of ν_{PJ}, initially chosen on the basis of dissociation energies, were then modified, sometimes considerably, by a comparison of calculated and observed dipole moments.

The IDME method differs from the Del Re method since it takes into consideration interactions between nonadjacent bonds. This means that the condition given by eq 18 does not have to be fulfilled to have the order of the inductive effects of the methyl and *tert*-butyl groups correctly reproduced. A vapor phase dielectric constant of 1.5 used in our calculations[28] indicates as well that parameters have to be somewhat changed in order to satisfy our calculations.

The IDME parameters have been chosen to reproduce the experimental dipole moments of a number of simple molecules as given in Table I, as well as some trends known from the ab initio charge distribution calculations where possible (Figure 1).

First, the δ°'s, which are correlated to electronegativities, were taken to be the same as in the Del Re parameters set. Then the γ's and ν's for the C–H and C–C bonds were modified so as to reproduce experimental and ab initio results from Table I and Figure 1. The γ's for the other bonds remained unchanged compared to the Del Re values, the only exception being the O–H bond. When one follows the condition imposed by Del Re method, that for atoms of the same rows γ should be the same, equal values of γ were assigned to the C–H and O–H bonds. Finally the ν's for the other bonds were modified by comparison of the calculated with observed dipole moments.

There are two bonds in the IDME parameter set (C—Br and C=O) that were not considered by Del Re.[20] The parameters here were determined by following the same procedure as for the other bonds. For instance, the δ°_{Br} has been taken to be equal to 0.3 considering the fact that bromine is slightly less electronegative than chlorine. The γ's were taken to be equal to the corresponding chlorine values on the basis of probable marked interaction of chlorine and bromine with carbon. The ν_{CBr} was then chosen to reproduce the experimental dipole moments of some bromine compounds, as given in Table I. The γ's for the C=O bond were taken to be the same as for the C—Cl and C—Br bonds, under the assumption that here, as well, a strong interaction between oxygen and carbon exists. The $\delta^\circ_{C=O}$ and $\nu_{C=O}$ were then chosen to reproduce the experimental dipole moments in a series of carbonyl compounds as given in Table I.

These parameters have been used to calculate bond dipole moments, the "permanent bond dipoles", that are input of the IDME program.[44] For CH_3Cl, for instance; the system of equations is written

$$\delta_C = \delta^\circ_C + 3\gamma_{C(H)}\delta_H + \gamma_{C(Cl)}\delta_{Cl}$$
$$\delta_H = \delta^\circ_H + \gamma_{H(C)}\delta_C$$
$$\delta_{Cl} = \delta^\circ_{Cl} + \delta_{Cl(C)}\delta_C$$

when δ's are calculated, the equations

$$Q_{CH} = (\delta_H - \delta_C)/2\nu_{CH}$$

$$Q_{CCl} = (\delta_{Cl} - \delta_C)/2\nu_{CCl}$$

are used to calculate bond charges (Q), and from the Q's and the bond lengths (R), bond dipole moments are calculated:

$$\mu_{CCl} = Q_{CCl}R_{CCl} \qquad \mu_{CH} = Q_{CH}R_{CH}$$

Although there is a degree of arbitrariness in these parameters they are so correlated that the change of one involves revision of the others, which strongly limits the arbitrariness. With the observed general good agreement between calculated and experimental moments and conformational energies (which will be discussed further in a subsequent paper), such an internal consistency strongly supports the reliability of the IDME method.

Conformational Energy Differences in the Vapor and in Solution

The purpose of the IDME method was to extend the molecular mechanics calculations to molecules containing two or more polar groups. It is obvious that in such compounds polar interactions are likely to be important. While such interactions have been considered in previous work, the level of this portion of the calculation was lower than for molecular mechanics calculations in general. The procedure that has been followed here was to calculate geometry and conformational energy (ΔE^t) by the present version of the molecular mechanics program (MM2)[21] with inclusion of the dipole–dipole interaction energy ($\Delta E_{\text{dipole–dipole}}$). The steric energy difference (ΔE_s) is then calculated from the difference $\Delta E_s = \Delta E^t - \Delta E_{\text{dipole–dipole}}$. The ΔE_s was then added to the charge interaction energy (ΔE_c) calculated by the IDME method. This gives the energy difference in the vapor (ΔE^v), the dielectric constant of which was taken[28] to be 1.5:

$$\Delta E^v = \Delta E_s(\text{MM2}) + \Delta E_c(\text{IDME}) \qquad (19)$$

In order to calculate conformational free energy difference in different solvents, (ΔG^s) the previously written "medium effect" (ME) program[22] was used. It gives the differences between the conformational free energy in the vapor (ΔG^v) and in solution (ΔG^s) by the following equation, which is based on the reaction field theory:

$$H(\text{ME}) = H_M - H_N = \Delta G^v - \Delta G^s = \text{DT} + \text{QT} = (KX/(\epsilon_2 - LX)) + (3hX/\epsilon_2(5 - X)) \qquad (20)$$

H(ME) is the solvation energy difference (calculated by the ME program), H_M and H_N being the solvation energies of two conformers M and N, $\text{DT} = \text{DT}_M - \text{DT}_N$ is a dipole term, $\text{QT} = \text{QT}_M - \text{QT}_N$ is a quadrupole term, and K is equal to $(\mu_M^2 - \mu_N^2)/d^3$ where μ_M and μ_N are molecular dipole moments of conformers M and N and d is a radius of a spherical cavity. The quantity h is

$$h_{MN} = \frac{3}{2d^5} \sum_{i,j=xyz}^{i \neq j} [4m_{ii}^2 + 3(m_{ij} + m_{ji})^2 - 4m_{ii}m_{jj}] \qquad (21)$$

$m_{ij} = \mu_i \times j$ etc., where $\mu_{x,y,z}$ and x, y, z, are components and coordinates of the bond dipole moments, ϵ_2 is a vapor dielectric constant, and L and X are given as follows:

$$X = (\epsilon - \epsilon_2)/(2\epsilon + \epsilon_2) \qquad L = 2(n^2 - 1)/(n^2 + 2) \qquad (22)$$

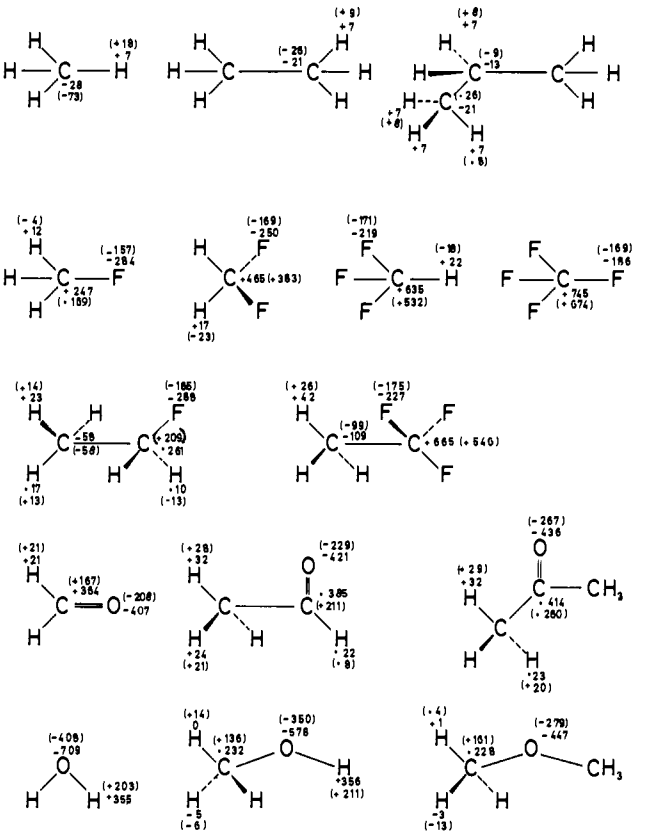


Figure 1. Charge distribution (10^{-3} electron) calculated by the IDME method and by the ab initio (STO-3G)[32] method (in parentheses).

where ϵ is a solvent dielectric constant and n is the solute refractive index.

The less polar solvents are simply considered to be continuous dielectric media. But with higher polar solvents, a more careful consideration of the solvent dipole interaction with the molecule is needed.

The new term (PT) was added to eq 20 to account for the solute–solvent, dipole–dipole, and quadrupole–dipole interactions. This term was introduced into solvation energy calculations by Abraham and Bretschneider.[33,34] It was modified to follow our assumption of a vapor dielectric constant (ϵ_2) of 1.5. The polar term (PT) is given by

$$\text{PT} = gf[1 - \exp(-gf/16RT)] \qquad (23)$$

where

$$g = \frac{3}{\epsilon_2 r^3}\left[\frac{2V_m RT}{\pi}\right]^{1/2}\left[\mu^2 + \frac{3m^2}{2r^2}\right]^{1/2}$$

The μ is the solute dipole moment and for our purposes may be considered to be the solute quadrupole moment. V_m is a solute molar volume, π and R are general constants, and T is temperature. The value r is the distance between solute and solvent dipoles. In our work it was taken to be equal to the sum of solute and solvent radii (d) calculated by the equation $d = (3M_w/4\pi\zeta)^{1/3}$, where M_w is the molecular weight and ζ is density. The f is defined by

$$f = [(\epsilon - 2)(\epsilon + 1)/\epsilon]^{1/2} \qquad (24)$$

where ϵ is a solvent dielectric constant.

The solvation energy difference between two conformers, H(ME) is now given by

$$H(\text{ME}) = \text{DT} + \text{QT} + \text{PT} \qquad (25)$$

(28) The vapor-phase dielectric constant of 1.5 is found empirically to be more satisfactory than 1.0 (vacuum), and the rational is that the molecule itself occupies much of the space between charges or dipoles. The dielectric constants of nonpolar molecules are about 2, for example (R. B. Hermann, *J. Org. Chem.*, **27**, 441 (1962)).

(29) C. Y. Chen and R. J. W. LeFèvre, *J. Chem. Soc.*, 3700 (1965).

(30) K. E. Calderbank, R. J. W. LeFèvre, and R. K. Pierens, *J. Chem. Soc. B*, 1608 (1970).

(31) A. B. Ramizov and M. L. Sverdlov, *Zh. Prikl. Spektrosk.*, **9** (1), 114 (1968).

(32) S. G. Vul'fson, I. M. Khamatullina, and A. N. Vereshchagin, *Izv. Akad. Nauk SSSR*, Ser. *Kim.* 1325 (1977).

(33) R. J. Abraham, *J. Phys. Chem.*, **73**, 1192 (1969).

(34) R. J. Abraham and E. Bretschneider in "Internal Rotation in Molecules", W. J. Orville-Thomas, Ed., Wiley, London, 1974.

Equation 25 was derived for the case of an arbitrary charge distribution in a spherical cavity immersed in a dielectric, the origin of the coordinate system being at the center of the charge.

Although the positioning of the origin of the coordinate system into the center of the volume[34,22] seemed satisfactory for the small molecules, we thought that it would be more realistic to place the origin at the center of charge. The derivation of the equations for the dipole (DT) and quadrupole (QT) terms requires that the dipole moment of the molecule be placed at the origin of the coordinate system. This condition is better fulfilled by placing the origin at the center of charge than by placing it at the center of volume, especially in the case of unsymmetrical molecules containing voluminous nonpolar groups.

It follows that the conformational free energy difference in solution is

$$\Delta G^s = \Delta G^v - H(\mathrm{ME}) = \Delta E_s(\mathrm{MM2}) + \Delta E_c(\mathrm{IDME}) - H(\mathrm{ME}) \quad (26)$$

The results of the calculations of ΔG^s and dipole moments are compared with experiment. Ilustrative results will be discussed below.

Dipole Moments and Charge Distribution

It may be seen from Table I that the changes of the dipole moments through each series of compounds is well reproduced. The calculated values of dipole moments are also in good agreement with experimental results.

Although there are no extensive systematic ab initio studies on charge distributions in saturated organic molecules, results are available[35,45] for some of the compounds in Table I and Figure 1. The 6-31G and 4-31G+BF results[45] are available only for methyl halides. The IDME charges reproduce the experimental dipole moments better than STO-3G and 4-31G calculations[35,45] do, but the general trends are quite similar.

The IDME calculations reveal that in propane a large negative charge is on the methyl carbon, and the same is obtained by ab initio (STO-3G) calculations. This is consistent with a small experimetal dipole moment of this compound.[36]

For the series water, methanol, methyl ether, etc., the agreement between the calculated and experimental dipole moments is very good, and the decrease in polarity with methyl substitution is well reproduced. The oxygen in methyl ether is substantially less negative than that in water.

The carbonyl series formaldehyde, acetaldehyde, and acetone also show the correct trend of increasing polarity with methyl substitution, and the dipole moments of these compounds are well calculated, as are those for the alkyl halides.

An inductive effect of the type $F^{\delta-} \leftarrow C^{\delta+} \leftarrow C^{\delta\delta+}$ might be expected in a compound like fluoroethane. On the contrary, ab initio[32] as well as CNDO/2 calculations[38] suggest an $F^{\delta-} \leftarrow C^{\delta+} \leftarrow C^{\delta\delta-}$ inductive effect, where the β-carbon is more negative than in ethane. While this result is not reproduced by the original Del Re method, the IDME method agrees with the ab initio type of charge distribution. The negative charge on the β-carbon increases when going from fluoroethane to the 1,1,1-trifluoroethane, which is again unexpected, from the usual interpretation of the inductive effect of the fluorine. While in the CNDO/2 calculations this was explained by back-donation from fluorine 2p π lone pairs, the IDME method indicates that this effect may partially be represented as due to the significant $H^+ \rightarrow C_\beta^-$ dipole moments induced by C–F bond dipole. The result is an increased negative charge on the β-carbon.

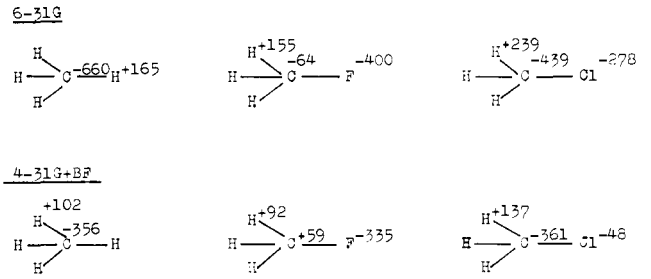


Figure 2. Charge distribution (10^{-3} electron) calculated by 6-31G[45] and 4-31G + BF[45] ab initio methods.

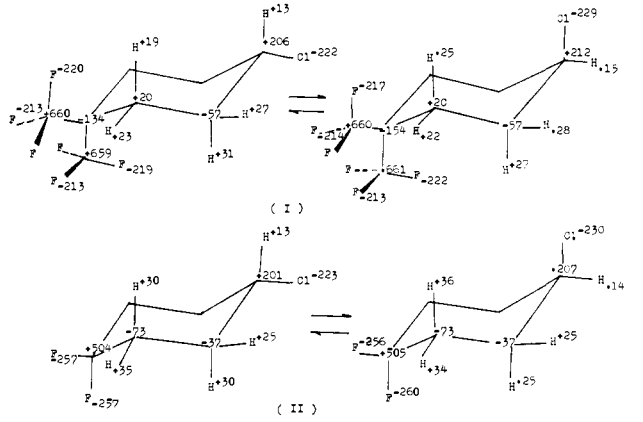


Figure 3. Charge distribution (10^{-3} electron) calculated by the IDME method.

The results obtained by ab initio 6-31G[45] and 4-31G + BF[45] methods for methyl halides (Figure 2) may, as well, be interpreted in the sense of the fluorine "back-donation effect."

The same effect is found, by ab initio[35,45] and CNDO/2[38] methods, to exist in the series of methyl fluorides. The IDME method gives different results since, for the compounds, it is reduced to the Del Re method where the usual interpretation of fluorine inductive effect $|F^{\delta-} \leftarrow C^{\delta+} \leftarrow C(H)^{\delta\delta+}|$ is built in the parameters set. The agreement of the IDME dipole moments of the fluorocarbons with experiment is very good.

Stolow et al.[46] concluded that the experimentally evaluated electrostatic components of the enthalpy differences between the two chair conformations of 4-chloro-1,1-bis(trifluoromethyl)-cyclohexane (I) and 4-chloro-1,1-difluorocyclohexane (II) are not consistent with charge alternation as predicted by CNDO/2 theory.

In contrast, the results reported here (Figure 3, Table IV, and Table V) are consistent with their experimental results for I and II. Although C-1 in I is negative and C-1···Cl interactions are more repulsive in the axial than in the equatorial conformation, they are counterbalanced by the other electrostatic interactions (Table IV). When all of the pairwise interactions in the molecule are taken into account, the electrostatic component of the conformational enthalpy change is correctly calculated (Table V). Besides, if for the vapor phrase we set $\Delta E = \Delta H = \Delta G$, which is reasonable approximation, our calculations reproduce well the shift of the conformational equilibrium of II when one goes from $CFCl_3$ to acetone[47] solvent (Table VI).

(35) W. J. Hehre and J. A. Pople, *J. Am. Chem. Soc.*, **92**, 2191 (1970).
(36) D. R. Lide, *J. Chem. Phys.*, **33**, 1514 (1960).
(37) A. L. McClellan, "Tables of Experimental Dipole Moments", W. H. Freeman and Co., San Francisco, 1963.
(38) J. A. Pople and M. Gordon, *J. Am. Chem. Soc.*, **89**, 4253 (1967).
(39) N. L. Allinger, J. Allinger, and N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 2926 (1960); N. L. Allinger, J. Allinger, L. A. Freiberg, R. Czaja, and N. A. LeBel, *ibid.*, 5876 (1960).
(40) J. Petrissans, S. Gromb, and J. Deschamps, *Bull. Soc. Chim. Fr.*, 4381 (1967).
(41) N. L. Allinger and H. M. Blatter, *J. Org. Chem.*, **27**, 1523 (1962).
(42) Y. H. Pan and J. B. Stothers, *Can. J. Chem.*, **45**, 2943 (1967).
(43) J. Cantacuzene, R. Jantzen and D. Ricard, *Tetrahedron*, **28**, 717 (1972).
(44) The description of the program is not included in this paper. The program will be submitted to the Quantum Chemistry Program Exchange and will be available from them later.
(45) K. B. Wiberg, *J. Am. Chem. Soc.*, **101**, 1718 (1979).
(46) R. D. Stolow, P. W. Samal, and T. W. Giants, *J. Am. Chem. Soc.*, **103**, 197 (1981).
(47) R. D. Stolow, T. W. Giants, and J. D. Roberts, *Tetrahedron Lett.*, 5777 (1968), and references cited therein.

Table III. The IDME Parameter Set

	bond (J–P)						
	C–H	C–C	C–O	O–H	C–F	C–Cl, C–Br	C=O
ν_{JP}	4.0	5.0	0.68	0.45	0.78	0.56, 0.54	0.68
$\gamma_{J(P)}$	0.1	0.1	0.1	0.1	0.1	0.2, 0.2	0.2
$\gamma_{P(J)}$	0.3	0.1	0.1	0.3	0.1	0.4, 0.4	0.4
σ^0_J	0.07	0.07	0.07	0.40	0.07	0.07, 0.07	0.07
σ^0_P	0.00	0.07	0.40	0.00	0.57	0.35, 0.30	0.70
LP[a]	0.64	0.99	0.89	0.43[b]	1.25	3.8 (2.9)[c]	5.3 (3.1),[c] 2.3
VP	0.64	0.27	0.46	0.43	0.40	1.85 (2.2)	2.7 (3.1), 1.4
TP	0.64	0.27	0.46	0.43	0.40	1.85 (2.2)	2.7 (3.1), 0.46
CR(J)	0.771	0.771	0.771	0.66	0.771	0.771	0.771, 0.771
CR(P)	0.30	0.771	0.66	0.30	0.64	0.99, 1.14	0.638

	bond (J–P)			bond (J–P)	
	O–lp	C–O		O–lp	C–O
DM(J–P)[d]	0.90	0.44	VP	0.0	0.46
LP	0.0	0.89	CR(J)	0.41	0.771
TP	0.0	0.46	CR(P)	0.25	0.41

[a] LP, TP, and VP are longitudinal, transverse, and vertical bond polarizabilities (in 10^{-24} cm^3).[23] CR(J) and CR(P) are covalent atomic radii (in 10^{-8} cm). [b] The value of the O-H longitudinal bond polarizability (*LP*) was taken from ref 17. We assumed LP = TP = VP. [c] These are the LP, TP, and VP values utilized for the C–X (X = Cl, Br) bond in case one of the bonds vicinal to C–X is polar as well; for instance: X–C–C–O, X–C–C=O, etc. The need for special values of LP, TP, and VP for the C–X bond in this case was noticed earlier. Chen and LeFevre[29] found the values of C–X (X = Cl, Br) bond polarizabilities, determined on isopropyl and *tert*-butyl halides or on monohalocyclohexanes, inadequate to reproduce experimental values of the molecular Kerr constants of 2-chloro- and 2-bromocyclohexanones. They had to make the C–X bond more isotropic, i.e., to assign smaller LP and larger TP and VP values to the C–X bond in these compounds relative to the values utilized for the C–X bond in halocyclohexane. The calculated values of the Kerr constant,[30] obtained with additive values of the C–Cl bond polarizabilities, determined on chlorocyclohexane, were unable to explain the equilibrium in 1,2-dihalocyclohexane without introducing twist-boat forms. The IR and Raman spectra[31] of this compound, however, may be fully interpreted by using only the chair conformations. This means that the use of the chlorocyclohexane LP, TP, and VP values for the C–Cl bond in the 1,2-dichlorocyclohexane is very likely inadequate. Similarly, molecular anisotropy and Kerr constants for some of the ortho-disubstituted benzenes[32] could not be reproduced by utilizing the C_{ar}–X (X = Cl, Br) bond polarizabilities determined on monosubstituted halobenzenes. Again more isotropic C–X bonds (smaller LP) had to be used. [d] Parameters for ethers when the lone pairs (lp) on oxygen were explicitly taken into account; DM(J-P) are bond dipole moments.

Table IV. Some of the Pairwise Electrostatic Interactions (E_{PJ}) Calculated for 1 by Using IDME Charges (kcal/mol)

interaction	E_{PJ} (1a)	E_{PJ} (1e)	ΔE_{PJ} (1a - 1e)	
C-1··Cl	1.98	1.60	0.38	
C-4··Cl	−6.01	−5.65	−0.36	
trans F_3C··Cl				
C··Cl	−6.48	−5.31	−1.17	
F··Cl	5.79	4.78	1.01	
			0.16	−0.42
cis F_3C··Cl				
C··Cl	−6.96	−6.18	−0.78	
F··Cl	6.32	5.80	0.52	
			−0.26	
C-2··Cl	−0.30	−0.24	−0.06	−0.12
C-6··Cl	−0.30	−0.24	−0.06	
cis H-2··Cl	−0.44	−0.23	0.21	−0.42
cis H-6··Cl	−0.44	−0.23	−0.21	

Table V. Electrostatic Component of the Conformational Energy Difference ($\Delta E_c = \Delta H_c$ kcal/mol)

	ΔE_c	
method	1e ⇌ 1a	11e ⇌ 11a
IDME	−1.06	−0.95
exptl[a]	−1.04 ± 0.07	−1.13 ± 0.14

[a] Reference 47.

Table VI. Conformational Energies ($\Delta E_c = \Delta H_c$ kcal/mol)

		calcd					obsd
solvent	ϵ	ΔE_s	ΔE_c	ΔE^v	H(ME)	ΔE	ΔG
			1e, 1a				
Vapor	1.5	0.43	−1.06	−0.63			
$CFCl_3$	2.28				−0.04	−0.59	−0.42[a]
acetone	20.7				−0.09	−0.54	
			11e, 11a				
Vapor	1.5	0.44	−0.96	−0.52			
CFCl	2.28				−0.15	−0.37	−0.50[a], −0.32[b]
acetone	20.7				−0.56	0.04	−0.16[c]

[a] Reference 46. [b] Reference 47, in propene solution. [c] Reference 47. ΔE_s is the steric energy difference, ΔE_c is the charge energy difference, ΔE^v is the total energy difference ($E_s + E_c$) in the vapor, H(ME) is the solvation effect, and ϵ is the dielectric constant.

Conclusion

The method used herein is sounder from a theoretical point of view than the procedures utilized previously for the treatment of electrostatic effects in molecular mechanics studies. The results obtained by the IDME method are, on the whole, rather similar to those obtained by the MSE method. The major exception is in the case of the 2,6-dihalocyclohexanones and 1,3-dichloro-5-methylcyclohexane, for which the conformational energies are much improved in the IDME calculation. In the subsequent paper, the IDME method will be applied to a number of polyfunctional halides, halo ketones, and halo ethers for the calculation of dipole moments and conformational energies, both in the gas phase and in solution.

(48) B. Franzus and B. E. Hudson, *J. Org. Chem.*, **28**, 2238 (1963).
(49) L. Došen-Mičović, D. Jeremić, and N. L. Allinger, *Tetrahedron*, **37**, 3455 (1981).